Connectivity-informed M/EEG inverse problem

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1 Introduction

Information between brain regions is transferred through white matter fibers with delays that are measurable with magnetoencephalography and electroencephalography (M/EEG) due to its millisecond temporal resolution. Therefore, a useful representation of the brain is that of a graph where its nodes are the cortical areas and edges are the physical connections between them: either local (between adjacent vertices on the cortical mesh) or non-local (long-range white matter fibers). These long-range anatomical connections can be obtained by diffusion MRI (dMRI) tractography, thus giving us an insight on interaction delays of the macroscopic brain network. A fundamental role in shaping the rich temporal structure of functional connectivity is played by the structural connectivity [6] that places constraints on which functional interactions occur in the network. In the context of regularizing the dynamics of M/EEG and recovering electrical activity of the brain from M/EEG measurements, traditional linear inverse methods deploy different constraints such as minimum norm, maximum-smoothness in space and/or time along the cortical surface. However, they usually do not take into account the structural connectivity and very few include delays supported by dMRI as a prior information [1]. The goal of this work is to include these delays into the MEG source reconstruction process by imposing temporal smoothness in structurally connected sources, with the corresponding delays. We propose to encapsulate delays provided by dMRI in a graph representation and show their potential in improving the MEG source reconstruction when compared to a state-of-the-art approach [4].

2 Forward and inverse M/EEG problem

Distributed source models place the current sources at a large number of vertices distributed on the cortex. The relationship between source amplitudes and M/EEG measurements is expressed by the linear model $\boldsymbol{M} = \boldsymbol{G}\boldsymbol{J} + \boldsymbol{E}$. The matrix of measurements is given by $\boldsymbol{M} \in \mathbb{R}^{N\times T}$ with N sensors and T time samples. The unknown matrix of S source amplitudes is given by $\boldsymbol{J} \in \mathbb{R}^{S\times T}$. The gain (lead field) matrix $\boldsymbol{G} \in \mathbb{R}^{N\times S}$ provides a linear relationship between source amplitudes and sensor data (a.k.a the M/EEG forward solution) and $\boldsymbol{E} \in \mathbb{R}^{N\times T}$ is additive noise. Recovering electrical activity of the brain from

M/EEG data is ill–posed and prior assumptions need to be introduced. A wide range of generalizations of minimum norm estimators [3] exist in the form

$$\min_{\boldsymbol{J}} U(\boldsymbol{J}) = \min_{\boldsymbol{J}} \{F(\boldsymbol{M}, \boldsymbol{J}) + \lambda P(\boldsymbol{J})\} = \min_{\boldsymbol{J}} \left\{ \|\boldsymbol{M} - \boldsymbol{G}\boldsymbol{J}\|_2^2 + \lambda \|\boldsymbol{W}\boldsymbol{J}\|_2^2 \right\} \quad (1)$$

which have a closed-form solution $\hat{\boldsymbol{J}} = \left(\boldsymbol{G}^{\boldsymbol{T}}\boldsymbol{G} + \lambda \boldsymbol{W}^{\boldsymbol{T}}\boldsymbol{W}\right)^{-1}\boldsymbol{G}^{\boldsymbol{T}}\boldsymbol{M}$. They differ by the choice of the matrix $\boldsymbol{W} \in \mathbb{R}^{S\times S}$ which incorporates a certain regularization property. However, all l_2-based inverse solvers suffer from smearing of even focal activation and often fail to exploit specific knowledge about the brain, such as the temporal dynamics of the underlying sources.

Laplacian as a smoothness constraint We can consider brain as a directed graph where its nodes are the current sources and its edges encode physical connection between them: either local (between adjacent vertices on the cortical mesh) or non-local (long-range white matter fibers). In the LORETA approach [5], similar activity is favoured between spatially adjacent vertices on the cortical mesh by choosing $\boldsymbol{W}$ to be the Laplacian matrix on the cortical surface, giving the solution with the maximum spatial smoothness. Since this approach does not account for long-range connectivity, it was extended in the Cortical Graph Smoothing (CGS) method [4] by forming a hybrid local/nonlocal connectivity graph with $\boldsymbol{A_{loc}}$ (spatial adjacency on the cortical surface) and $\boldsymbol{A_{tr}}$ (tractography-based connectivity matrix). They are used to form local $\boldsymbol{L_{loc}}$ and tractography-based $\boldsymbol{L_{tr}}$ graph Laplacians, resulting in the penalty term $P_{CGS}(\boldsymbol{J}) = \lambda_{loc}\boldsymbol{J}^{\boldsymbol{T}}\boldsymbol{L_{loc}}\boldsymbol{J} + \lambda_{tr}\boldsymbol{J}^{\boldsymbol{T}}\boldsymbol{L_{tr}}\boldsymbol{J}$. This way CGS penalizes the weighted sum of squared differences in activity between connected cortical patches.

2.1 Connectivty-Informed MEG Inverse Problem (CIMIP)

While previous approaches exploited structural connectivity between different cortical areas, transmission delays were not taken into account. In order to enforce temporal smoothness between the time courses of connected sources, we incorporated a modified version of the Laplacian operator as a penalty term in the minimization. We can consider all time samples in a single large problem as $\boldsymbol{m} = \tilde{\boldsymbol{G}}\boldsymbol{j} + \boldsymbol{\epsilon}$ where $\boldsymbol{m} \in \mathbb{R}^{NT}$ and $\boldsymbol{j} \in \mathbb{R}^{ST}$ are vectors of concatenated measurements and source intensities, $\tilde{\boldsymbol{G}} = diag(\boldsymbol{G}, ...\boldsymbol{G}) \in \mathbb{R}^{NT\times ST}$ and $\boldsymbol{\epsilon} \in \mathbb{R}^{NT}$ is additive noise. To recover electrical activity of the brain, we minimize the following objective function

$$U_{\text{CIMIP}}(\boldsymbol{j}) = \|\boldsymbol{m} - \tilde{\boldsymbol{G}}\boldsymbol{j}\|_2^2 + \lambda(\boldsymbol{j}^{\boldsymbol{T}}\tilde{\boldsymbol{L}}\boldsymbol{j})^2 \quad (2)$$

Firstly, a binary time-dependent connectivity graph $\tilde{\boldsymbol{A}} = \tilde{\boldsymbol{A}}_{\boldsymbol{loc}} + \tilde{\boldsymbol{A}}_{\boldsymbol{tr}}$ is built. Short-range connections are encapsulated in $\tilde{\boldsymbol{A}}_{\boldsymbol{loc}} = diag(\boldsymbol{A_{loc}}, ...\boldsymbol{A_{loc}}) \in \mathbb{R}^{ST\times ST}$. In order to include connections for different delays, we build a tractography-based graph $\tilde{\boldsymbol{A}}_{\boldsymbol{tr}} \in \mathbb{R}^{ST\times ST}$ where nonzero elements designate the presence of a long-range connection *for a specific delay*, which was not considered in the CGS. The output of dMRI tractography is a set of streamlines representing the white matter fiber bundles. Given the streamline lengths and the information conduction speed, we can calculate the propagation delays for each connection. In accordance to recent findings [2] showing that the proportionality between fiber diameter and conduction velocity is $6.67ms^-1/\mu m$ and previous works of [1], information conduction speed is assumed to be constant across brain and equal to $6m/s$. Using $\tilde{\boldsymbol{A}}$, the matrix $\tilde{\boldsymbol{L}}$ in (2) is a regularization matrix defined as $\tilde{\boldsymbol{L}} = \boldsymbol{I} - \tilde{\boldsymbol{A}}$. This is a symmetric block matrix where each block corresponds to a specific delay. In the standard Laplacian the sum of each row is 0, so the preferred solutions would be the ones where all connections of a given node have the same amplitude. For that reason, we used $\tilde{\boldsymbol{L}}$ in order to favour solutions where the activity of a source is equal to the sum of activities of its connections.

3 Data simulation

Source-level brain activity is modelled as a function of its local and long-range connections as a multivariate autoregressive (MAR) model. The source space was parcellated into 68 neuroanatomical regions of interest. Assuming that only a few regions are typically active during a cognitive task, the activity is simulated for 10 randomly chosen subnetworks as a graph path with different lengths, so the number of active regions varied from 2 to 5. Two types of simulations were performed: multiple focal sources and multiple spread sources. In the first, only the sources in the active region that have a long-range connection in the next active region were assigned the activity. In the latter, this activity was also spread to its adjacent neighbours. The activity was propagated between sources that share a long-range connection, with an appropriate delay.

4 Results

Results of the reconstruction of brain activity from simulated MEG measurements were compared to the CGS method. Source estimation performance was evaluated with the same metric as in [4], by identifying the largest local maxima of the estimated current sources. Peak localization error was computed as the Euclidean distance between local spatial maxima k^* of simulated (GT) and reconstructed (REC) sources i.e. $d(k^*) = |k^*_{REC} - k^*_{GT}|$

Table 1. Mean and standard deviation of peak localization errors (in mm)

Method	Multiple focal sources	Multiple spread sources
CGS	48.09 ± 17.98	53.03 ± 17.2
CIMIP	28.05 ± 8.4	27.99 ± 6.97

5 Conclusion

Our preliminary results show that including the conduction delays provided by dMRI encapsulated in a graph representation improves MEG source localization when compared to the CGS method. Future work will examine the performance on real MEG data and comparison to other methods.

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